In the Claims

The following amendments are made with respect to the claims in the International application PCT/EP2005/000873.

This listing of claims will replace all prior versions and listings of claims in this application.

1 (currently amended). ~~Method~~ A method for identifying and quantifying tumour-associated peptides, comprising the steps:

> providing a first sample of tissue or cells,
>
> providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,
>
> obtaining peptides from the first and the second sample,
>
> separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,
>
> mixing of the so modified peptides from both samples,
>
> determining the amino acid sequences of the peptides, and
>
> determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics.

2 (currently amended). ~~Method~~ The method according to claim 1, characterised in that the peptides from both samples are chemically modified by using at least two different stable isotopes of the same element.

3 (currently amended). ~~Method~~ The method according to claim 1[[or 2]], characterised by the following steps:

a)   providing a sample from tumourous and a sample from corresponding healthy tissue or accordingly transfected or infected cell lines, wherein both samples have identical amounts per weight or cellular counts,

b)   isolating peptides from said sample from tumourous tissue,

c)   isolating peptides from said sample from corresponding healthy tissue,

d)   chemically modifying the peptides obtained in step (b) with a chemical group that contains a stable isotope of an element from the periodic system of the elements,

e)   chemically modifying the peptides obtained in step (c) with a chemical group that contains a second stable isotope of the element from the periodic system of the elements used in step d),

f)   mixing of the chemically modified peptides obtained from steps (d) and (e),

g)   separating the peptides obtained from step f) by a chromatographic method,

h)   identifying and determining peptides having identical amino acid sequences and the ratio by weight of chemically modified peptides with identical amino acid sequences from step (g),

i)   identifying tumour-associated peptides that are suitable, ~~preferably particularly suitable for the~~ for combination into a therapeutic vaccine, based on the data obtained from step (h).

4 (currently amended).   ~~Method according to any of claims 1 to 3~~ The method according to claim 1, characterised in that the tumour-associated peptides are MHC-class I-ligands.

5 (currently amended).   ~~Method~~ The method according to claim 3[[or 4]], characterised in that in step d) deuterium (^2D) and in step e) regular hydrogen (^1H) are used as stable isotopes.

6 (currently amended).   ~~Method according to any of claims 3 to 5~~ The method according to claim 3, characterised in that in step g) a chromatographic separation of the peptides by HPLC is performed.

7 (currently amended).   ~~Method according to any of claims 3 to 6~~ The method according to claim 3, characterised in that step h) is performed by mass spectrometric analysis.

8 (currently amended).   ~~Method~~The method according to claim 7, characterised in that the mass spectrometric analysis for determining the amount ratios of the two peptides with identical amino acid sequence and identical chemical modification is performed

based on at least two different isotopes of the same element from the periodic system of elements.

9 (currently amended). ~~Method~~ The method according to claim 8, characterised in that the relative intensity of the signals as measured for peptides having identical amino acid sequence and identical chemical modification but different isotopes of the same element that are simultaneously present is used for calculating the relative quantitative ratio between said peptides.

10 (currently amended). ~~Method according to any of claims 3 to 9~~ The method according to claim 3, characterised in that in step i) suitable databases for the identification of tumour-associated genes and gene products are used.

11 (currently amended). ~~Method according to any of claims 3 to 10~~ The method according to claim 3, characterised in that following step h) an additional step is performed, wherein the reactivity of peripheral leukocytes~~, preferably of T-lymphocytes,~~ against the identified and quantified peptides is tested.

12 (currently amended). ~~Method~~ The method according to claim 11, characterised in that the testing of the reactivity takes place by measuring the cytokine-mRNA and/or interferon-mRNA that is synthesised by the leukocytes.

13 (currently amended). ~~Method~~ The method according to claim 11, characterised in that the testing of the reactivity takes place by the activation of peripheral T-lymphocytes by means of reconstituted complexes from antigen-presenting molecules and peptides.

14 (currently amended). ~~Method~~ The method according to claim 13, characterised in that the complexes of antigen-presenting molecules and peptides that are used for activating T-lymphocytes are fixed on a surface.

15 (currently amended). ~~Method~~ The method according to claim 14, characterised in that the surface that is used for fixing said complexes of antigen-presenting molecules and peptides consists of polystyrol.

16 (currently amended). ~~Method according to any of claims 13 to 15~~ The method according to claim 13, characterised in that the antigen presenting molecules are coupled by chemical reaction with biotin, and the surface that is used is made from polystyrol being coated with streptavidin by a chemical reaction.

17 (currently amended). ~~Method~~ A method for producing a peptide, wherein a peptide is identified ~~according to the method according to any of claims 1 to 16~~ by a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics;

and wherein the identified peptide is synthesised chemically, in vitro or in vivo.

18 (currently amended). ~~Peptide~~ A peptide, wherein the peptide is identified ~~according to~~ by a method ~~according to any of claims 1 to 16 and/or produced according to a method according to claim 17~~ comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics;

and/or wherein said peptide is produced according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a

tumour-associated peptide having an amino acid sequence that is selected from the group consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a molecule of the human major histocompatibility complex (MHC) class-I.

19 (canceled).

20 (currently amended). ~~Peptide~~ The peptide according to claim 18[[or 19]], characterised in that at least one amino acid is replaced by another amino acid having similar chemical characteristics.

21 (currently amended). ~~Peptide~~ The peptide according to ~~any of claims 18 to 20~~ claim 18, characterised in that at least one additional amino acid is present at the N- or C-terminus.

22 (currently amended. ~~Peptide~~ The peptide according to ~~any of claims 18 to 21~~ claim 18, characterised in that at least one amino acid is deleted.

23 (currently amended). ~~Peptide~~ The peptide according to ~~any of claims 18 to 22~~ claim 18, characterised in that at least one amino acid is chemically modified.

24 (currently amended). ~~Use of one or several of the peptides according to any of claims 18 to 23 for~~ A method for producing a medicament for the treatment of tumourous diseases and/or adenomatous diseases wherein said method comprises the use of a peptide, or a polynucleotide encoding the peptide, wherein the peptide is identified according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics;

and/or wherein said peptide is produced according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a

tumour-associated peptide having an amino acid sequence that is selected from the group
consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a
molecule of the human major histocompatibility complex (MHC) class-I.

25 (currently amended).   ~~Use of the peptide according to any of claims 18 to 23~~ A method for
the treatment of tumourous diseases and/or adenomatous diseases wherein said
method comprises administering, to a patient in need of such treatment, a peptide, or a
polynucleotide encoding said peptide, wherein said peptide is
identified according to a method comprising the steps:
providing a first sample of tissue or cells,
providing a second sample of tissue or cells with the identical amount by weight or
cellular count as the first sample,
obtaining peptides from the first and the second sample,
separately, chemically identically modifying the peptides from both samples in order
to generate different physical characteristics in the peptides from the different
samples,
mixing of the so modified peptides from both samples,
determining the amino acid sequences of the peptides, and
determining the relative amount ratios of peptides from both samples having identical
sequences, based on the different physical characteristics
and/or wherein said peptide is produced according to a method comprising the steps:
providing a first sample of tissue or cells,
providing a second sample of tissue or cells with the identical amount by weight or
cellular count as the first sample,
obtaining peptides from the first and the second sample,
separately, chemically identically modifying the peptides from both samples in order
to generate different physical characteristics in the peptides from the different
samples,
mixing of the so modified peptides from both samples,
determining the amino acid sequences of the peptides, and
determining the relative amount ratios of peptides from both samples having identical
sequences, based on the different physical characteristics,
and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a
tumour-associated peptide having an amino acid sequence that is selected from the group
consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a
molecule of the human major histocompatibility complex (MHC) class-I.

26 (currently amended). [[Use]] The method according to claim 24[[or 25]], characterised in
that the disease is renal, lung, colon, stomach, pancreatic, breast, prostate, ovarian
and/or skin cancer.

27 (currently amended). [[Use]] The method according to any of claims 24 to 26 claim 25,
characterised in that the peptide is used together with an adjuvans adjuvant.

28 (currently amended). Use according to any of claims 24 to 27 The method according to
claim 25, characterised in that a peptide bound to an antigen presenting cell is used.

29 (currently amended). Use of the peptide according to any of claims 18 to 23 A method for
the labelling of leukocytes, in particular of T-lymphocytes, evaluating the progress of
therapy in a tumourous disease, or producing an antibody; wherein said method
comprises the use of a peptide, wherein the peptide is identified by a method
comprising the steps:
providing a first sample of tissue or cells,
providing a second sample of tissue or cells with the identical amount by weight or
cellular count as the first sample,
obtaining peptides from the first and the second sample,
separately, chemically identically modifying the peptides from both samples in order
to generate different physical characteristics in the peptides from the different
samples,
mixing of the so modified peptides from both samples,
determining the amino acid sequences of the peptides, and
determining the relative amount ratios of peptides from both samples having identical
sequences, based on the different physical characteristics;
and/or wherein said peptide is produced according to a method comprising the steps:
providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or

cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order

to generate different physical characteristics in the peptides from the different

samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical

sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a

tumour-associated peptide having an amino acid sequence that is selected from the group

consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a

molecule of the human major histocompatibility complex (MHC) class-I.

30 (canceled).

31 (canceled).

32 (currently amended). ~~Pharmaceutical composition, containing one or several peptides~~

~~according to any of claims 18 to 23~~ A pharmaceutical composition comprising a

pharmaceutically acceptable carrier and a peptide wherein the peptide is identified

according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or

cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order

to generate different physical characteristics in the peptides from the different

samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics;

and/or wherein said peptide is produced according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a

tumour-associated peptide having an amino acid sequence that is selected from the group consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a molecule of the human major histocompatibility complex (MHC) class-I.

33 (currently amended).   ~~Nucleic~~ A nucleic acid molecule~~, encoding the peptide according to any of claims 18 to 23~~ that encodes a peptide wherein the peptide is identified according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics;

and/or wherein said peptide is produced according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a

tumour-associated peptide having an amino acid sequence that is selected from the group consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a molecule of the human major histocompatibility complex (MHC) class-I.

34 (currently amended). ~~Vector,~~ A vector comprising ~~the nucleic acid molecule according to claim 33~~ a nucleic acid molecule encoding a peptide wherein the peptide is identified according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical

sequences, based on the different physical characteristics;

and/or wherein said peptide is produced according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or

cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order

to generate different physical characteristics in the peptides from the different

samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical

sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a

tumour-associated peptide having an amino acid sequence that is selected from the group

consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a

molecule of the human major histocompatibility complex (MHC) class-I.

35 (currently amended). ~~Cell that was~~ A cell that is genetically modified with ~~the aid of the~~

~~nucleic acid molecule according to claim 33 or with the vector according to claim 34~~

~~in such a manner that it expresses a peptide according to any of claims 18 to 23~~ a

nucleic acid molecule encoding a peptide wherein the peptide is identified according

to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or

cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order

to generate different physical characteristics in the peptides from the different

samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical

sequences, based on the different physical characteristics;

and/or wherein said peptide is produced according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or

cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order

to generate different physical characteristics in the peptides from the different

samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical

sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a

tumour-associated peptide having an amino acid sequence that is selected from the group

consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a

molecule of the human major histocompatibility complex (MHC) class-I.

36 (canceled).

37 (currently amended). ~~Method~~ A method for producing a vaccine with the steps:

a)   performing ~~the methods according to any of claims 1 to 16~~ a method for identifying

and quantifying tumour-associated peptides, comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or

cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order

to generate different physical characteristics in the peptides from the different

samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics,

b) producing the identified ~~peptides~~ peptide(s), and

c) formulating the produced ~~peptides~~ peptide(s) into the vaccine.

38 (currently amended). ~~Diagnostic~~ A diagnostic method, wherein ~~the method according to any of claims 1 to 16 is performed,~~ a first method for identifying and quantifying tumour-associated peptides is performed comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics

and wherein the presence and/or the amount ratio of a peptide is used as a diagnostic marker.

39 (currently amended). ~~Method~~ A method for treatment of a pathological condition, wherein an immune response against a protein of interest is triggered, characterised in that a therapeutic effective amount of at least one ~~of the peptides according to any of claims 18 to 23~~ peptide is administered wherein the peptide is identified by a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics;

and/or wherein said peptide is produced according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a tumour-associated peptide having an amino acid sequence that is selected from the group consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a molecule of the human major histocompatibility complex (MHC) class-I is administered.

40 (currently amended). ~~Electronic~~ An electronic storage medium containing the amino acid sequence of at least one [[of]] peptide, wherein the peptide is identified by a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics;

and/or wherein said peptide is produced according to a method comprising the steps:

providing a first sample of tissue or cells,

providing a second sample of tissue or cells with the identical amount by weight or cellular count as the first sample,

obtaining peptides from the first and the second sample,

separately, chemically identically modifying the peptides from both samples in order to generate different physical characteristics in the peptides from the different samples,

mixing of the so modified peptides from both samples,

determining the amino acid sequences of the peptides, and

determining the relative amount ratios of peptides from both samples having identical sequences, based on the different physical characteristics,

and the identified peptide is synthesised chemically, in vitro or in vivo;

and/or wherein said peptide is a tumour-associated peptide having an amino acid sequence that is selected from the group consisting of SEQ ID-No. 1 to 36, wherein said peptide has the ability to bind to a molecule of the human major histocompatibility complex (MHC) class-I; the peptides according to any of claims 18 to 23 and/or the electronic storage medium contains the nucleic acid sequence of the nucleic acid molecule according to claim 33 a molecule that encodes one of said peptides.